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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,655	04/27/2001	Wei Huang	LJL 357	9013

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KOLISCH, HARTWELL, DICKINSON,
McCORMACK & HEUSER
520 S.W. Yamhill Street, Suite 200
Portland, OR 97204

EXAMINER

CHEU, CHANGHWA J

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 11/03/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.

09/844,655

Applicant(s)

HUANG ET AL.

Examiner

Jacob Cheu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 94-105 and 108-115 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 94-105 and 108-115 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 15.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Applicant's amendment filed on July 30, 2003 has been received and entered into record and considered.

The following information provided in the amendment affects the instant application:

1. Claims 1-93, 106, 107 are cancelled.
2. Claims 94-105, 108-115 are currently under examination.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.
2. Claims 94-105, 108-115 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to claim 94, line 6, "product of the operation of the enzyme" is vague and indefinite. It is unclear what kind of "operation" applicant refers, e.g. phosphorylation or decyclization. Similarly, claim 115 shares the same problem as claim 94.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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4. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 94-101, 108, 110, 112-115 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nikiforov (USP 6472141) in view of Posewits et al. (Anal. Chem. 1999, Vol. 7: 2883-2892).

Nikiforov teaches a fluorescence polarization assay to determine the enzymatic operation of a phosphorylatable compound, i.e. activity of phosphatase (dephosphorylate) or kinase (phosphorylate) on the polypeptide substrate. (Col. 3, line 7-20) Nikiforov teaches the steps of conducting the assay includes, first contacting the substrate with the enzyme, then adding a second mixture binding molecule, i.e. proteins (macromolecule) containing metal ion selected from Fe³⁺, Ca²⁺, Ni²⁺ and Zn²⁺, and detecting the difference of luminescence polarization emitted from the sample. (supra; Col. 7, line 15-27) Nikiforov teaches that the bound fluorescent molecules show higher fluorescent polarization compared to the unbound molecules, and there is no need of separation of the unbound from the bound molecules for calculation. (supra and the equation (2)) Nikiforov teaches that the product can be fluorescently labeled, i.e. luminescent. (claim 18) It is inherent that the phosphorylatable compounds taught by Nikiforov are products of posttranslational modification in the biological system. The binding molecule taught by Nikiforov, e.g. protein, could be viewed as a nanoparticle. *Supra*. The method taught by Nikiforov also can be applied for screening inhibitors or enhancers of the enzymes. (Col. 7, lines 36-40) Nikiforov also teaches high-throughput, i.e. mass sample array, for the fluorescent polarization method. (Col. 21, line 17-22; Col. 24, line 18-20; Col. 25, line 3-

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6) However, Nikiforov does not specifically teach using gallium (Ga) metal ion for its fluorescent polarization assay.

Posewitz et al teach using gallium (Ga) rendering more selective and efficient results over the choice of Fe^{3+} , or Al^{3+} in purification of phosphopeptides molecule. (See Abstract, and page 2892, Left Col. Second paragraph) Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to replace the conventional metal ions of Fe^{3+} , or Al^{3+} for capturing phosphopeptides as taught by Nikiforov with the Ga ion as taught by Posewitz et al. with a reasonable expectation of success. The motivation to do so would have been the recognition of the following: (1) Fe^{3+} and Ga ion have been recognized possessing similar behavior in the ion binding proteins (Posewitz et al. reference, page 2892, Right Column, first paragraph; Figure 3); (2) Ga ion may substitute Fe^{3+} in study ion binding protein mechanism, *supra*; (3) Ga ion has been shown more selective and efficient metal ion for targeting phosphopeptides. *Supra*.

With respect to claim 113, where the recited binding coefficient is no longer than about 10^{-8} M. It would have been obvious to one having ordinary skill in the art at the time the invention was made to optimize the binding assay, since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 105 USPQ 233.

Allowable Subject Matter

6. Claims 102-105, 109, 111 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: The closest prior arts taught by Nikiforov and Posewitz et al. as discussed *supra* disclose a fluorescence polarization assay to determine the enzymatic activity of an enzyme operating on a substrate by use of a metal ion, e.g. Gallium. Both Nikiforov and Posewitz

et al. teach using this method on kinase and phosphatase, but not on phosphodiesterase as recited in this application. Furthermore, the substrate for the phosphodiesterase is nucleotide, which is chemically and biologically distinct from the polypeptides used in both Nikiforov and Posewits' reference. Therefore, prior arts neither teach nor suggest use fluorescence polarization coupling with the Gallium ion to determine the activity of phosphodiesterase.

Response to Applicant's Arguments

7. The rejections of claims 94-101, 108, 110, 112-115 under 35 U.S.C. 103(a) as being unpatentable over Nikiforov in view of Posewits et al., are maintained.

Applicant argues that the Posewits et al. reference "implies" that Ga binds phosphopeptides less avidly than Fe, thus applicant believes that Posewits et al. teach away from replacing Fe with Ga in fluorescence polarization. (See Amendment, page 9, first paragraph; Posewits et al. reference Figure 3) Applicant's arguments have been considered but are not persuasive. Figure 3 of Posewits et al. reference shows the comparison of retention-elution of phosphopeptides from Ga microtips v. Fe microtips. The black bars indicate that both Ga and Fe have similar retention capacity. The similar retention capacity of phosphopeptide with the Ga and Fe provides the motivation and expectation of success that both Fe and Ga can be interchangeably served as binding partners in the fluorescence polarization assay. With respect to the elution argument, this step does not have bearing with the instant invention because (1) no step of elution is required in the instant invention; (2) no addition of elution reagent, e.g. sodium phosphate, is needed. Accordingly, Posewits et al. reference does teach the similar binding capacity of Ga and Fe with phosphopeptides and provide the motivation and suggestion of using Ga as a binding partner for phosphopeptides.

With respect to the second argument on the unexpected *benefit* to use Ga instead of Fe in fluorescence, applicant asserts that replacing Fe with Ga produces better polarization

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results, i.e. less quenching. Applicant's argument has been considered but appears not convincing. Posewits et al. reference teaches using Ga as a binding partner for phosphopeptide. Nikiforov reference teaches using Fe, Al, Ni, Ca polycationic component as the binding partners bound to the phosphorylated product for polarization fluorescence assay. (See claims 1, 8, 12, 13) It would have been obvious to one having ordinary skill in the art at the time the invention was made to have provided Nikiforov with the Ga metal to achieve the results as the instant invention taught by Posewits et al. with a reasonable expectation of success since using Ga for phosphopeptide binding is known in the art, and alternative replacement of Fe for polarization fluorescence assay appears obvious, and a better result is within expectation of an artisan in the field.

Conclusion

8. No claim is allowed.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jacob Cheu whose telephone number is 703-306-4086. The examiner can normally be reached on 9:00-5:00.

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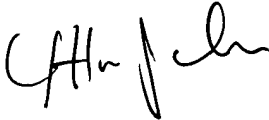
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 703-305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-305-3399.

Jacob Cheu

Examiner

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October 22, 2003



LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

10/21/03